JP 62-192322 A for case 10/519,484
(JP 2001-048807) Machine Translation

[Claim(s)]
[Claim 1]A tablet which dissolves a slightly soluble medicine in water by an acetyl tryptophan or its salt permitted pharmacologically and/or saccharin, or its salt permitted pharmacologically and polyethylene glycol.
[Claim 2]The aqueous formulation according to claim 1 containing following ingredient A-D.
A. A slightly soluble medicine B. acetyl tryptophan or its salt permitted pharmacologically and/or saccharin, or its salt C. polyethylene glycol D. water soluble polymer permitted pharmacologically [Claim 3]A water soluble polymer A methylcellulose, hydroxypropyl methylcellulose, The aqueous formulation according to claim 2 which is at least one chosen from salt with which salt and chitosan by which a polyvinyl alcohol, a polyvinylpyrrolidone, alginic acid, or alginic acid is permitted pharmacologically, or chitosan is permitted pharmacologically.
[Claim 4]The aqueous formulation according to claim 2 whose water soluble polymers are a methylcellulose and/or the hydroxypropyl methylcellulose.
[Claim 5]The aqueous formulation according to claim 1 to 4 whose pH is 5.5-10.0.
[Claim 6]The aqueous formulation according to claim 1 to 5 in which a slightly soluble medicine was chosen from an antifungal, synthetic antimicrobials, an anti herpes virus agent, an antiplatelet agent, an $alpha_1$ blocker, carbonate dehydrarase inhibitor, and adrenocortical steroid and which is a kind at least.
[Claim 7]The aqueous formulation according to claim 6 in which a slightly soluble medicine was chosen from dipyridamole, norfloxacin, ofloxacin, and lomefloxacin hydrochloride and which is a kind at least.
[Claim 8]The aqueous formulation according to claim 1 to 7 whose dosage form is oral administration liquid medicine, injection, an ear drop, a nasal drop, ophthalmic solution, nebula, or vapor.

[Detailed Description of the Invention]
[0001]
[Industrial Application]This invention relates to the aqueous formulation of a slightly soluble medicine. By this invention, an acetyl tryptophan or its salt permitted pharmacologically and/or saccharin, or its salt and polyethylene glycol (it calls for short following PEG) which are permitted pharmacologically are contained in more detail. Therefore, when medicating a living body with the slightly soluble medicine represented by dipyridamole, it is related with the tablet which dissolved in water in the desirable pH range.

[0002]
[Description of the Prior Art]Dipyridamole is marketed as an oral administration agent and injection now as a therapeutic drug of angina, myocardial infarction, ischemic heart disease, and a congestive heart disease. When eyewash is applied in the solution of dipyridamole, it is known that a strong intraocular pressure descent operation will be acquired (JP,7-258084,A), and the ophthalmic solution of dipyridamole is expected as a new glaucoma remedy. Generally it is known from a point of the stimulus of as opposed

to an eye in pH of the ophthalmic solution that 5-8 are preferred and it is 6-8 more preferably (JP,7-258084,A and the 13th game of Pharmacopoeia of Japan). It is supposed from the field of the stimulus also as injection that not separating not much greatly is more desirable than neutrality as for pH (the 13th game of Pharmacopoeia of Japan). However, since the solubility to the water of dipyridamole in the above neutral vicinity is very low, it is difficult to prepare the ophthalmic solution and the injection in neutral vicinity as a tablet which dipyridamole dissolved in water in respect of preservation stability. Also in JP,7-258084,A, the dipyridamole ophthalmic solution which adjusted pH to 3-5 is only indicated. Since it is such, a tablet excellent in the preservation stability which a suitable quantity of dipyridamole dissolved in water in neutral vicinity is desired.
[0003]as a procedure of dissolving dipyridamole in water in neutral vicinity, the procedure of adding an acetyl tryptophan or a tryptophan is indicated -- **** (JP,8-143475,A). When this invention persons evaluated the solubility of dipyridamole by an acetyl tryptophan, it became clear that the crystal deposition of dipyridamole happens at an early stage comparatively. International application PCT/JP99/03107 has disclosed in order to obtain the aqueous formulation which dissolved the slightly soluble medicine represented by dipyridamole in water in neutral vicinity, use the synergistic solubilization effect of polysorbate and/or polyoxyethylene hydrogenated castor oil, a methylcellulose, and/or the hydroxypropyl methylcellulose. It is indicating solubilizing a slightly soluble medicine still more nearly synergistically by blending PEG with the above-mentioned composition. However, the solubilization effect of an acetyl tryptophan or saccharin is not indicated at all.
[0004]Using a tryptophan or saccharin for Andrew X. Chen's and others report (Pharm. Pes., 1994, 11 (3), p398-401) as a dissolving method of a nucleoside derivative is indicated. However, about the solubilization effect of an acetyl tryptophan, it is unstated in any way. It is unstated in any way also about the synergistic solubilization effect by using PEG and saccharin together. WO99/6447 has disclosed the aqueous formulation which contains an acetyl tryptophan and/or saccharin, and those salts permitted pharmacologically and water soluble polymers as crystal deposition inhibitor of the antivirotic which has a pudding frame or a pyrimidine frame. However, it is not indicated at all by blending a still more specific water soluble polymer with PEG, the acetyl tryptophan, and/or saccharin in which a synergistic solubilization effect is shown that a still more nearly synergistic solubilization effect is shown.
[0005]
[Means for solving problem]That is, the purpose of this invention is to obtain the aqueous formulation which dissolved the slightly soluble medicine represented by dipyridamole in water in neutral vicinity by using the synergistic solubilization effect of an acetyl tryptophan and/or saccharin as shown in Embodiment 1, and PEG. When a specific water soluble polymer is blended with the above-mentioned composition, as Embodiments 2 and 4 or 5 showed, in order that the solubility to the water of a slightly soluble medicine may improve still more nearly synergistically, desirable aqueous formulation is obtained. Since the aqueous formulation of this invention is prepared in desirable pH region when it excels in preservation stability and medicates a living body, it is expected that the stimulativeness at the time of medication will be low. Since the slightly soluble medicine is dissolving in water unlike a suspension tablet, it does not need to be anxious about the deposition to the foreign body sensation at the time of the medication which has been a

problem with a suspension tablet, the dispersion of the dose, and the container of a suspended substance, etc.
[0006]
[Embodiment of the Invention]This invention is explained in detail below. Although the usefulness of effect is expected, since it is refractory in water in neutral vicinity, the slightly soluble medicine used for this invention refers to that to which the use is restricted. Such a medicine For example, an antifungal, for example, fluconazole, clotrimazole, Isoconazole nitrate, econazole nitrate, miconazole nitrate, bifonazole, etc., Synthetic antimicrobials, for example, ofloxacin, ciprofloxacin hydrochloride, tosufloxacin tosilate, Norfloxacin, lomefloxacin hydrochloride, PAZUFUROKISASHIN, etc., An anti herpes virus agent, for example, acyclovir, ganciclovir, idoxuridine, Cilostazol, antiplatelet agents, for example, dipyridamole, such as vidarabine, etc., An alpha$_1$ blocker, for example, prazosin hydrochloride, bunazosin hydrochloride, terazosin hydrochloride, etc., Carbonate dehydrarase inhibitor, for example, acetazolamide, methazolamide, etc., The salt with which these medicines are permitted pharmacologically, such as adrenocortical steroid, for example, difluprednate, budesonide, diflucortolone valerate, hydrocortisone butyrate propionate, clobetasone butyrate, and fluorometholone, is mentioned.
[0007]Any of D- which is an optical isomer, L-, and DL-object may be used for an acetyl tryptophan, and those salt permitted pharmacologically may be used for it. As these salt permitted pharmacologically, sodium salt, potassium salt, calcium salt, etc. can be illustrated. The salt permitted pharmacologically, for example, sodium salt, potassium salt, calcium salt, etc. may be similarly used about saccharin. As saccharin, from Daito Chemicals, Daiwa Chemicals, Inc., and Ocean Chemical industry, as saccharin sodium, it is marketed from Fuji Amide Chemicals, Daito Chemicals, Daiwa Chemicals, Inc., Ocean Chemical industry, and Tanabe Seiyaku Co., Ltd., and is easily available. The schema of acetyl tryptophan sodium and saccharin sodium, specifications, a use, the amount used, and a brand name are indicated in detail in the excipient encyclopedia (Japanese excipient association edit, Yakuji Nippo issue). Although these acetyl tryptophan, saccharin, or those salt permitted pharmacologically may be used independently, the effect that it is more nearly synergistic to use together and use is acquired, and it is more preferred.
[0008][PEG used for this invention] From Wako Pure Chemical Industries, Ltd. again by the brand name of PEG-200, -300, -600, -1000, -1540, -2000, -4000, -6000, -20000, -50000, -200000, and 400000 [-] The macrogol 200, -300, -400, -It is sold from Nippon Oil & Fats Co., Ltd. by the brand name of 600, -1000, -1540, -4000, -6000, and 20000 [-]. Although there is no restriction in particular in the weight average molecular weight of PEG used for this invention, 400-50000 are preferred and 1000-especially 20000 are preferred. Since the osmotic pressure of aqueous formulation does not become not much high when weight average molecular weight is 400 or more, it is desirable, and since the viscosity in a liquid state does not become high too much when weight average molecular weight is 50000 or less, it is desirable. It is also possible to mix two or more sorts of PEG(s), and to adjust weight average molecular weight to above-mentioned optimum within the limits. A schema, specifications, a use, the amount used, a brand name, etc. of PEG are indicated in detail in the excipient encyclopedia (Japanese excipient association edit, Yakuji Nippo issue).
[0009]It is possible by blending a still more specific water soluble polymer with the

above-mentioned acetyl tryptophan and/or saccharin, and PEG to raise the solubility over the water of a slightly soluble medicine synergistically. The salt etc. with which salt and chitosan by which a methylcellulose, the hydroxypropyl methylcellulose, a polyvinyl alcohol, a polyvinylpyrrolidone, alginic acid, and alginic acid are pharmacologically permitted as a water soluble polymer used by this invention, and chitosan are permitted pharmacologically are mentioned. They are a methylcellulose or the hydroxypropyl methylcellulose especially preferably also in this. As salt with which alginic acid is permitted pharmacologically, sodium salt, potassium salt, calcium salt, etc. can be illustrated. A hydrochloride, a sulphate, etc. can be illustrated as salt with which chitosan is permitted pharmacologically. if the viscosity at 20 ** of the 2% solution is a thing of the 13 - 12000 mPa-s range, any MC of the methylcellulose (it is hereafter called MC for short) used for this invention is independent -- or it can be mixed and used. The content of a methoxyl group has 26 to 33% of preferred range from a soluble viewpoint over water. MC is distinguished with the viscosity of the solution, for example, there is a thing of the display viscosity 15, 25, 100, 400, 1500, and 8000 (a number is mPa-s of the 20 ** viscosity of 2% solution) in the variety of a commercial item. [the hydroxypropyl methylcellulose (it is hereafter called HPMC for short) used for this invention] According to the above-mentioned excipient dictionary, it is divided into three kinds (2208, 2906, and 2910) by the content of the methoxyl group and a hydroxypropyl group, It is distinguished with the viscosity of the solution further, respectively, for example, there is a thing of the display viscosity 4-100000 (a number is mPa-s of the 20 ** viscosity of 2% solution) in the variety of a commercial item, and it is easily available. HPMC used by this invention has a with a display viscosity [the point of handling to] of 10000 or less preferred thing. As a polyvinyl alcohol, as Gosenol, the Nippon Synthetic Chemical Industry Co., Ltd. It is marketed from Unitika, Ltd. as Kuraray Co., Ltd. and Unitika poval as DENKI KAGAKU KOGYO K.K. and Kuraray PVA as Shin-Etsu Chemical Co., Ltd. and the electrification PVA as Shin-etsu poval, and is easily available. Sodium arginine is marketed from Henkel Hakusui, Inc. and Ajinomoto Co., Inc. as KIBUN FOOD CHEMIFA CO., LTD. and TEKISAMIDO as Kimitsu Chemical industry and duck algin as KIMITSU algin, and is easily available. Polyvinylpyrrolidone K25, K30, and K90 are marketed from ISP, Inc. and Gokyo Industry Corp. as BASF Japan, Ltd. and a plus boss as Kollidon (registered trademark), and, as for a polyvinylpyrrolidone, are easily available. A schema, specifications, a use, the amount used, a brand name, etc. of the above-mentioned water soluble polymer are indicated in detail in the excipient encyclopedia.

[0010]As an embodiment of the slightly soluble medicine content aqueous formulation of this invention, a slightly soluble medicine, an acetyl tryptophan and/or saccharin, and the density range of PEG are limited by the following Reasons. If the concentration of a slightly soluble medicine is a range which the target drug effect is obtained and can be prepared as aqueous formulation, there will be no restriction in particular. For example, the concentration of dipyridamole (it is hereafter called DPY for short) is usually 0.001 - 0.5 W/V%, and is 0.005 - 0.1 W/V% preferably. At less than 0.5 W/V%, since the concentration of DPY dissolves completely [DPY / water], it is preferred. When the concentration of DPY is 0.001W/V % or more, since sufficient drug effect is expectable, it is desirable. For example, the concentration of synthetic antimicrobials, such as norfloxacin, ofloxacin, and lomefloxacin hydrochloride, is usually 0.01-3W/V%. When

concentration is less than 3 W/V%, since a medicine dissolves in water completely, it is desirable. When concentration is 0.01W/V % or more, since sufficient drug effect is expectable, it is desirable. The operating concentration of an acetyl tryptophan or saccharin is usually 0.01 - 20 W/V%. At less than 20 W/V%, since osmotic pressure does not become high too much, concentration is preferred. In order to dissolve the slightly soluble medicine of a quantity required to obtain drug effect, it is preferred that concentration is more than 0.01 W/V%. The operating concentration of PEG is usually 0.1 - 10 W/V%. Since it is in the range which the viscosity of aqueous formulation tends to deal with when the concentration of PEG is less than 10 W/V%, it is desirable. In order to dissolve the slightly soluble medicine of a quantity required to obtain drug effect, it is preferred that concentration is more than 0.1 W/V%.

[0011]Although not limited especially as operating concentration of a water soluble polymer, the concentration from which the viscosity of about 2-1000 mPa-s is obtained is preferred, and it is the concentration from which the viscosity of the viscosity about 2 - 100 mPa-s is obtained more preferably. When METOROZU (registered trademark) SM-15 by Shin-Etsu Chemical [Co., Ltd.] Co., Ltd. is used as a methylcellulose, for example, about 0.5 to 3%, When METOROZU (registered trademark) 60SH50 by Shin-Etsu Chemical [Co., Ltd.] Co., Ltd. is used as hydroxypropyl methylcellulose and the polyvinyl alcohol 1000 (partial saponification type) is used as a polyvinyl alcohol about 0.5 to 2%, about 1 to 5% is desirable.

[0012]The aqueous formulation of this invention is usually adjusted to pH 5-10, and is preferably adjusted to pH 5.5-8.0 from the point of the stimulus at the time of medication.

[0013]In order to adjust pH of the aqueous formulation of this invention, various pH adjusters usually added are used. As acids, ascorbic acid, hydrochloric acid, a gluconic acid, acetic acid, lactic acid, boric acid, phosphoric acid, sulfuric acid, tartaric acid, citric acid, etc. are mentioned, for example. As bases, a potassium hydroxide, a calcium hydroxide, sodium hydroxide, magnesium hydroxide, monoethanolamine, diethanolamine, triethanolamine, etc. are mentioned, for example. As other pH adjusters, amino acid, such as a glycine, a histidine, and epsilon-aminocaproic acid, is mentioned.

[0014]In preparing the aqueous formulation of this invention, an isotonizing agent, a preservative, a preservative, etc. which can be permitted pharmacologically can be added to the aqueous formulation of this invention in the range which does not spoil the effect of this invention if needed. As an isotonizing agent, saccharides, such as xylitol, a mannitol, and grape sugar, propylene glycol, glycerin, sodium chloride, potassium chloride, etc. are mentioned. As a preservative, invert soap, such as benzalkonium chloride, benzethonium chloride, and chlorhexidine glyconate, The Para hydroxybenzoic acid methyl, the Para hydroxybenzoic acid propyl, Organic acids, such as alcohols, such as paraben, such as Para hydroxybenzoic acid butyl, chlorobutanol, phenylethyl alcohol, and benzyl alcohol, sodium dehydroacetate, a sorbic acid, and a potassium sorbate, and the salts of those can be used. Stabilizing agents, such as EDTA and those salt permitted pharmacologically, a tocopherol and its inductor, and a sodium sulfite, are mentioned as other additive agents.

[0015]The aqueous formulation of this invention can perform heat sterilization processing by the filter sterilization by a membrane filter, the pressurization heat sterilization by autoclave, the fractional sterilization, etc. The eye dropper made from plastics can be filled up with the aqueous formulation of this invention, and it can be used

as ophthalmic solution. Since this is saved over a long period of time, pillow packing may be carried out at the lamination bag of a polyethylene film and aluminum foil with a deoxidizer (for example, ageless (registered trademark) and Mitsubishi Gas Chemical Co., Inc.). The dropping bottle made from plastics can be filled up with the aqueous formulation of this invention, and it can be used as an ear drop. The quantum nebulizer for noses can be filled up with the aqueous formulation of this invention, and it can be used as a nasal drop. Aqueous formulation of this invention is ****(ed) after filling up an ampul, and can be used as injection (intravenous injection, an intra-arterial injection, a subcutaneous injection, intradermal injection, an intramuscular injection, the injection in a spine cavity, intraperitoneal injection, intra-ocular injection, etc.), oral administration liquid medicine, the vapor, and nebula. In the case of oral administration liquid medicine, in the case of a plastics medicine manufacture bottle and the vapor, this is filled up with and used for an atomizer etc. according to direction for use in the case of an electromotive nebulizer and the nebula.

[0016]Illustration of preparation of DPY content aqueous formulation will add and agitate DPY, PEG, and saccharin sodium to sterile purified water. Acids are added here, and it mixes until each ingredient dissolves. After adding what dissolved the water soluble polymer in sterile purified water and mixing well, by adding bases, it adjusts to predetermined pH and sterile purified water adjusts in predetermined capacity. If necessary, various kinds of additive agents, for example, a buffer, an isotonizing agent, a preservative, a stabilizing agent, etc. can be added. Prepared DPY content aqueous formulation can be used as the DPY content ophthalmic solution by filling up a plastic character instillation bottle after filter sterilization.

[0017]Although an embodiment is given to below and this invention is explained to it still in detail, the range of this invention is not limited.

[0018]0.05 g DPY, saccharin and Na 0.4 g, and PEG4000 [4.8-g] (macrogol 4000 and Nippon Oil & Fats Co., Ltd.) were added and agitated to embodiment 1 sterile-purified-water 50mL. It added and dissolved until pH became three or less about the hydrochloric acid of 1N here. 0.5 more g of epsilon-aminocaproic acid was added, and the churning dissolution was carried out. NaOH of 1N or the hydrochloric acid of 1N adjusted pH to 5.5, and it was made 100mL by adding sterile purified water. The prepared liquid was filtered with the membrane filter with the aperture of 0.45 micrometer, the vial was filled up, and it was considered as the aqueous formulation (formula No.1) of this invention. The DPY aqueous formulation for comparison (formula No.2 and 3) which does not add either of saccharin and Na, or PEG4000 was prepared by the same procedure to the DPY aqueous formulation of this invention as comparison. 0.05 g DPY and PEG4000 [2.4-g] were added and agitated to sterile-purified-water 50mL. It added and dissolved until pH became three or less about the hydrochloric acid of 1N here. It is 25 W/V% acetyl tryptophan solution (method of preparation: it dissolved by adding 25 g of N-acetyl-L-tryptophan to sterile-purified-water 50mL, and adding NaOH of 5N.) to a pan. The hydrochloric acid of 3N was added here and pH was set to 100mL with sterile purified water after adjusting to 5.6. 0.8mL was added, 0.5 g of epsilon-aminocaproic acid was added after mixture, and the churning dissolution was carried out. NaOH of 1N or 1N hydrochloric acid adjusted pH to 5.5, and it was made 100mL by adding sterile purified water. The prepared liquid was filtered with the membrane filter with the aperture of 0.45 micrometer, the vial was filled up, and it was considered as the aqueous formulation

(formula No.4) of this invention. The DPY aqueous formulation for comparison (formula No.5 and 6) which does not add an acetyl tryptophan or either of PEG4000 was prepared by the same procedure to the DPY aqueous formulation of this invention as comparison. Each prepared DPY aqueous formulation was kept at 25 **, and time until the crystal of DPY deposits was measured. And the following (1) type estimated the solubilization effect in the slightly soluble medicine of this invention.
Crystal deposition retardation degree = (A - (B+C)) *100 /(B+C) (1) A : In the aqueous formulation (a) of this invention, Time C until a slightly soluble medicine deposits in a time B:comparison tablet (b) until a slightly soluble medicine deposits: Time until a slightly soluble medicine deposits in a comparison tablet (c) (b and c shall not contain either in the additive agent of a)
When preparation of a tablet was impossible, the value put into A, B, and C was set to 0. (1) Since the solubilization effect in the aqueous formulation of this invention is higher than what **(ed) and united the solubilization effect of the comparison tablet when the degree of crystal deposition retardation for which it asked by the formula shows a positive value, the synergistic solubilization effect is shown. Since the solubilization effect in the aqueous formulation of this invention is equivalent to what **(ed) and united the solubilization effect of the comparison tablet when the degree of crystal deposition retardation is 0, the additive solubilization effect is shown. Since the aqueous formulation of this invention is lower than what **(ed) and united the solubilization effect of the comparison tablet when the degree of crystal deposition retardation shows a negative value, decreasing the solubilization effect of a comparison tablet is shown. The result examined by the above-mentioned appraisal method about the prepared aqueous formulation (formula No.1-6) was shown in table-1. It is shown that each degree of crystal deposition retardation of the aqueous formulation of this invention becomes a positive big value, and has a strong synergistic solubilization effect. That is, it was shown that the solubilization effect over the slightly soluble medicine of saccharin or an acetyl tryptophan (it is hereafter called AcTrp for short), and PEG is synergistic.
[0019]
[Table-1]

表－1

No.	1	2	3
区分	本発明	比較例	比較例
DPY (w/v%)	0.05	0.05	0.05
サッカリン・Na (w/v%)	0.4	0.4	-
PEG4000 (w/v%)	4.8	-	4.8
ε-アミノカプロン酸 (w/v%)	0.5	0.5	0.5
NaOH、HCl	適量	適量	適量
pH	5.5	5.5	5.5
調製時の性状	黄色澄明	黄色澄明	調製不可
結晶析出遅延度	1350		

No.	4	5	6
区分	本発明	比較例	比較例
DPY (w/v%)	0.05	0.05	0.05
AcTrp (w/v%)	0.2	0.2	-
PEG4000 (w/v%)	2.4	-	2.4
ε-アミノカプロン酸 (w/v%)	0.5	0.5	0.5
NaOH、HCl	適量	適量	適量
pH	5.5	5.5	5.5
調製時の性状	黄色澄明	黄色澄明	調製不可
結晶析出遅延度	200		

[0020]0.05 g DPY, saccharin and Na 0.2 g, and PEG4000 [2.4-g] were added and agitated to embodiment 2 sterile-purified-water 50mL. It added and dissolved until pH became three or less about the hydrochloric acid of 1N here. 12.5mL and 0.5 g of epsilon-aminocaproic acid were added, and the churning dissolution of what dissolved MC (SM-15, METOROZU (registered trademark), and Shin-etsu Chemicals) in sterile purified water so that it might become 4 W/V% was carried out. NaOH of 1N or the hydrochloric acid of 1N adjusted pH to 5.5, and it was made 100mL by adding sterile purified water. The prepared liquid was filtered with the membrane filter with the aperture of 0.45 micrometer, the vial was filled up, and it was considered as the aqueous formulation (formula No.7) of this invention. The DPY aqueous formulation for comparison (formula No.8 and 9) which does not add either of saccharin Na and PEG4000 or SM-15 was prepared by the same procedure to the DPY aqueous formulation of this invention as comparison. 0.05 g DPY and PEG4000 [2.4-g] were added and agitated to sterile-purified-water 50mL. It added and dissolved until pH became three or less about the hydrochloric acid of 1N here. After mixture, 12.5mL and 0.5 g of epsilon-aminocaproic acid were added, and the churning dissolution of 4 W/V%SM-15 was carried out until it carried out 0.8mL addition of the 25 W/V%AcTrp solution and became uniform at the pan. NaOH of 1N or 1N hydrochloric acid adjusted pH to 5.5, and it was made 100mL by adding sterile purified water. The prepared liquid was filtered with the membrane filter with the aperture of 0.45 micrometer, the vial was filled up, and it was considered as the aqueous formulation (formula No.10) of this invention. The DPY aqueous formulation for comparison (formula No.4 and 9) which does not add either one of AcTrp, PEG4000 or SM-15 was prepared by the same procedure to the DPY aqueous formulation of this invention as comparison. Time until the crystal of DPY deposits was measured about each prepared DPY aqueous formulation. And the same procedure as Embodiment 1 estimated the solubilization effect

over the slightly soluble medicine of this invention, and the result was shown in table-2. It is shown that each degree of crystal deposition retardation of the aqueous formulation of this invention becomes a positive big value, and has a strong synergistic solubilization effect. That is, it was shown that the solubilization effect over the slightly soluble medicine of saccharin or AcTrp, PEG, and MC is synergistic.

[0021]

[Table-2]

表－２

No.	7	8	9
区分	本発明	比較例	比較例
DPY (w/v%)	0.05	0.05	0.05
サッカリン・Na (w/v%)	**0.2**	**0.2**	-
PEG4000 (w/v%)	**2.4**	**2.4**	-
SM-15 (w/v%)	**0.5**	-	**0.5**
ε-アミノカプロン酸 (w/v%)	0.5	0.5	0.5
NaOH、HCl	適量	適量	適量
pH	5.5	5.5	5.5
調製時の性状	黄色澄明	黄色澄明	調製不可
結晶析出遅延度	717		

No.	10	4	9
区分	本発明	比較例	比較例
DPY (w/v%)	0.05	0.05	0.05
AcTrp (w/v%)	**0.2**	**0.2**	-
PEG4000 (w/v%)	**2.4**	**2.4**	-
SM-15 (w/v%)	**0.5**	-	**0.5**
ε-アミノカプロン酸 (w/v%)	0.5	0.5	0.5
NaOH、HCl	適量	適量	適量
pH	5.5	5.5	5.5
調製時の性状	黄色澄明	黄色澄明	調製不可
結晶析出遅延度	978		

[0022]0.05 g DPY, saccharin and Na 0.2 g, and PEG4000 [2.4-g] were added and agitated to embodiment 3 sterile-purified-water 50mL. It added and dissolved until pH became three or less about the hydrochloric acid of 1N here. After mixture, 12.5mL and 0.5 g of epsilon-aminocaproic acid were added, and the churning dissolution of 4 W/V%SM-15 was carried out until it carried out 0.8mL addition of the 25 W/V%AcTrp solution and became uniform at the pan. NaOH of 1N or 1N hydrochloric acid adjusted pH to 5.5, and it was made 100mL by adding sterile purified water. The prepared liquid was filtered with the membrane filter with the aperture of 0.45 micrometer, the vial was filled up, and it was considered as the aqueous formulation (formula No.11) of this invention. The DPY aqueous formulation for comparison (formula No.7 and 10) which does not add either one of AcTrp or saccharin was prepared by the same procedure to the DPY aqueous formulation of this invention as comparison. Time until the crystal of DPY deposits was measured about each prepared DPY aqueous formulation. And the same procedure as Embodiment 1 estimated the solubilization effect over the slightly soluble medicine of this invention, and the result was shown in table-3. It is shown that the degree of crystal deposition retardation of the aqueous formulation of this invention becomes a positive big value, and has a strong synergistic solubilization effect. That is, when PEG and MC existed, it was shown that the solubilization effect over the slightly soluble medicine of saccharin and AcTrp is synergistic.

[0023]
[Table-3]
表－3

No.	11	7	10
区分	本発明	比較例	比較例
DPY (w/v%)	0.05	0.05	0.05
サッカリン・Na (w/v%)	0.2	0.2	-
AcTrp (w/v%)	0.2	-	0.2
PEG4000 (w/v%)	2.4	2.4	2.4
SM-15 (w/v%)	0.5	0.5	0.5
ε-アミノカプロン酸 (w/v%)	0.5	0.5	0.5
NaOH、HCl	適量	適量	適量
pH	5.5	5.5	5.5
調製時の性状	黄色澄明	黄色澄明	黄色澄明
結晶析出遅延度	437		

[0024]0.3 g of norfloxacin (it is hereafter called NFLX for short) and PEG4000 [2.4-g] were added and agitated to embodiment 4 sterile-purified-water 50mL. It added and dissolved until pH became five or less about the hydrochloric acid of 1N here. NaOH of 1N or 1N hydrochloric acid adjusted pH to 7.0 after mixture until it carried out 2.4mL addition of the 25 W/V%AcTrp solution and became uniform at the pan, and it was made 100mL by adding sterile purified water. The prepared liquid was filtered with the membrane filter with the aperture of 0.45 micrometer, the vial was filled up, and it was considered as the aqueous formulation (formula No.12) of this invention. The NFLX aqueous formulation for comparison (formula No.13 and 14) which does not add either of AcTrp or PEG4000 was prepared by the same procedure to the NFLX aqueous formulation of this invention as comparison. 0.3 g NFLX and PEG4000 [2.4-g] were added and agitated to sterile-purified-water 50mL. It added and dissolved until pH became five or less about the hydrochloric acid of 1N here. 5mL addition of 1.2mL and 4 W/V%SM-15 was carried out for 25 W/V%AcTrp solution at the pan, and it mixed until it became uniform. NaOH of 1N or 1N hydrochloric acid adjusted pH to 7.0, and it was made 100mL by adding sterile purified water. The prepared liquid was filtered with the membrane filter with the aperture of 0.45 micrometer, the vial was filled up, and it was considered as the aqueous formulation (formula No.15) of this invention. The NFLX aqueous formulation for comparison (formula No.16 and 17) which does not add either one of AcTrp, PEG4000 or SM-15 was prepared by the same procedure to the NFLX aqueous formulation of this invention as comparison. Time until the crystal of NFLX deposits was measured about each prepared NFLX aqueous formulation. And the same procedure as Embodiment 1 estimated the solubilization effect over the slightly soluble medicine of this invention, and the result was shown in table-4. It is shown that each degree of crystal deposition retardation of the aqueous formulation of this invention becomes a positive big value, and has a strong synergistic solubilization effect. That is, as Embodiment 2 also showed, it was shown that the solubilization effect over the slightly soluble medicine of AcTrp, PEG, and MC is synergistic.
[0025]
[Table-4]

表－4

No.	12	13	14
区分	本発明	比較例	比較例
NFLX (w/v%)	0.3	0.3	0.3
AcTrp (w/v%)	0.6	0.6	-
PEG4000 (w/v%)	2.4	-	2.4
NaOH、HCl	適量	適量	適量
pH	7.0	7.0	7.0
調製時の性状	無色澄明	無色澄明	調製不可
結晶析出遅延度	67		

No.	15	16	17
区分	本発明	比較例	比較例
NFLX (w/v%)	0.3	0.3	0.3
AcTrp (w/v%)	0.3	0.3	-
PEG4000 (w/v%)	2.4	-	2.4
SM-15 (w/v%)	0.2	-	0.2
NaOH、HCl	適量	適量	適量
pH	7.0	7.0	7.0
調製時の性状	無色澄明	調製不可	無色澄明
結晶析出遅延度	875		

[0026]0.05 g DPY, saccharin and Na 0.2 g, and PEG4000 [2.4-g] were added and agitated to embodiment 5 sterile-purified-water 50mL. It added and dissolved until pH became three or less about the hydrochloric acid of 1N here. 12.5mL and 0.5 g of epsilon-aminocaproic acid were added, and the churning dissolution of 4 W/V%SM-15 was carried out. NaOH of 1N or the hydrochloric acid of 1N adjusted pH to 5.5, and it was made 100mL by adding sterile purified water. The prepared liquid was filtered with the membrane filter with the aperture of 0.45 micrometer, the vial was filled up, and it was considered as the aqueous formulation (formula No.7) of this invention. The DPY aqueous formulation for comparison (formula No.8 and 9) which does not add either of saccharin Na and PEG4000 or SM-15 was prepared by the same procedure to the DPY aqueous formulation of this invention as comparison. Instead of carrying out 12.5mL addition of 4 W/V%SM15, the DPY content aqueous formulation (formula No.18) of this invention which carried out 40mL addition of what dissolved HPMC (60SH50, METOROZU (registered trademark), and Shin-etsu Chemicals) in sterile purified water so that it might become 1.25 W/V% was prepared. As comparison, the DPY aqueous formulation for comparison (formula No.19) which does not add the saccharin Na and PEG4000 was prepared. instead of carrying out 12.5mL addition of 4W/V%SM15 -- a polyvinyl alcohol (the polyvinyl alcohol 1000 and a partial saponification type.) Wako Pure Chemical Industries, Ltd. and the following PVA -- calling for short -- the DPY content aqueous formulation (formula No.20) of this invention which carried out 40mL addition of what was dissolved in sterile purified water so that it might become 1.25 W/V% was prepared. As comparison, the DPY aqueous formulation for comparison (formula No.21) which does not add the saccharin Na and PEG4000 was prepared. instead of carrying out 12.5mL addition of 4W/V%SM15 -- a polyvinylpyrrolidone (Kollidon (registered trademark) K25 and BASF Japan, Ltd..) the following PVP -- calling for short -- the DPY content aqueous formulation (formula No.22) of this invention which carried out 40mL addition of what was dissolved in sterile purified water so that it might become 1.25 W/V% was prepared. As comparison, the DPY aqueous

formulation for comparison (formula No.23) which does not add the saccharin Na and PEG4000 was prepared. Instead of carrying out 12.5mL addition of 4 W/V%SM15, the DPY content aqueous formulation (formula No.24) of this invention which carried out 40mL addition of what dissolved alginic acid and Na (Wako Pure Chemical Industries, Ltd.) in sterile purified water so that it might become 1.25 W/V% was prepared. As comparison, the DPY aqueous formulation for comparison (formula No.25) which does not add the saccharin Na and PEG4000 was prepared. Instead of carrying out 12.5mL addition of 4 W/V%SM15, the DPY content aqueous formulation (formula No.26) of this invention which carried out 40mL addition of what dissolved chitosan (the chitosan 10 and Wako Pure Chemical Industries, Ltd.) in sterile purified water so that it might become 1.25 W/V% was prepared. As comparison, the DPY aqueous formulation for comparison (formula No.27) which does not add the saccharin Na and PEG4000 was prepared. Instead of carrying out 12.5mL addition of 4 W/V%SM15, the DPY content aqueous formulation (formula No.28) which carried out 40mL addition of what dissolved a chondroitin sulfuric acid and Na (Wako Pure Chemical Industries, Ltd.) in sterile purified water so that it might become 1.25 W/V% was prepared. As comparison, the DPY aqueous formulation (formula No.29) which does not add the saccharin Na and PEG4000 was prepared. Instead of carrying out 12.5mL addition of 4 W/V%SM15, the DPY content aqueous formulation (formula No.30) which carried out 40mL addition of what dissolved a hyaluronic acid and Na (HIARURONSAN HA-Q and Kewpie) in sterile purified water so that it might become 1.25 W/V% was prepared. As comparison, the DPY aqueous formulation (formula No.31) which does not add the saccharin Na and PEG4000 was prepared. Instead of carrying out 12.5mL addition of 4 W/V%SM15, the DPY content aqueous formulation (formula No.32) which carried out 40mL addition of what dissolved the carboxyvinyl polymer (high screw WAKO 104 and Wako Pure Chemical Industries, Ltd.) in sterile purified water so that it might become 0.25 W/V% was prepared. As comparison, the DPY aqueous formulation (formula No.33) which does not add the saccharin Na and PEG4000 was prepared. Time until the crystal of DPY deposits was measured about each prepared DPY aqueous formulation. And the same procedure as Embodiment 1 estimated the solubilization effect over the slightly soluble medicine of this invention, and the result was shown in table-5. It was MC, HPMC, PVA, PVP, alginic acid and Na, and chitosan that the degree of crystal deposition retardation became a positive value in the added water soluble polymer. That is, it was shown that saccharin, and PEG(s) and these water soluble polymers have a synergistic solubilization effect to a slightly soluble medicine. In particular, it was shown that the synergistic effect of MC and HPMC is strong. A chondroitin sulfuric acid and Na, a hyaluronic acid and Na, or the degree of crystal deposition retardation of the carboxyvinyl polymer became a negative value, and it was shown that addition of these water soluble polymers decreases the solubilization effect of saccharin and PEG. That is, when it blended with saccharin and PEG, it was shown that it is a certain specific water soluble polymer that a synergistic solubilization effect is acquired to a slightly soluble medicine.

[0027]

[Table-5]

表－5

No.	7	9	18	19
区分	本発明	比較例	本発明	比較例
DPY（w/v%）	0.05	0.05	0.05	0.05
サッカリン・Na（w/v%）	0.2	-	0.2	-
PEG4000（w/v%）	2.4	-	2.4	-
水溶性高分子の種類	MC	MC	HPMC	HPMC
水溶性高分子の濃度（w/v%）	0.5	0.5	0.5	0.5
ε-アミノカプロン酸（w/v%）	0.5	0.5	0.5	0.5
NaOH、HCl	適量	適量	適量	適量
pH	5.5	5.5	5.5	5.5
調製時の性状	黄色澄明	調製不可	黄色澄明	調製不可
結晶析出遅延度	717		667	

No.	20	21	22	23
区分	本発明	比較例	本発明	比較例
DPY（w/v%）	0.05	0.05	0.05	0.05
サッカリン・Na（w/v%）	0.2	-	0.2	-
PEG4000（w/v%）	2.4	-	2.4	-
水溶性高分子の種類	PVA	PVA	PVP	PVP
水溶性高分子の濃度（w/v%）	0.5	0.5	0.5	0.5
ε-アミノカプロン酸（w/v%）	0.5	0.5	0.5	0.5
NaOH、HCl	適量	適量	適量	適量
pH	5.5	5.5	5.5	5.5
調製時の性状	黄色澄明	調製不可	黄色澄明	調製不可
結晶析出遅延度	433		150	

No.	24	25	26	27
区分	本発明	比較例	本発明	比較例
DPY（w/v%）	0.05	0.05	0.05	0.05
サッカリン・Na（w/v%）	0.2	-	0.2	-
PEG4000（w/v%）	2.4	-	2.4	-
水溶性高分子の種類	ｱﾙｷﾞﾝ酸・Na	アルギン酸・Na	キトサン	キトサン
水溶性高分子の濃度（w/v%）	0.5	0.5	0.5	0.5
ε-アミノカプロン酸（w/v%）	0.5	0.5	0.5	0.5
NaOH、HCl	適量	適量	適量	適量
pH	5.5	5.5	5.5	5.5
調製時の性状	黄色澄明	調製不可	黄色澄明	調製不可
結晶析出遅延度	25		25	

No.	28	29	30	31
区分	比較例	比較例	比較例	比較例
DPY（w/v%）	0.05	0.05	0.05	0.05
サッカリン・Na（w/v%）	0.2	-	0.2	-
PEG4000（w/v%）	2.4	-	2.4	-
水溶性高分子の種類	ｺﾝﾄﾞﾛｲﾁﾝ硫酸・Na	ｺﾝﾄﾞﾛｲﾁﾝ硫酸・Na	ﾋｱﾙﾛﾝ酸・Na	ﾋｱﾙﾛﾝ酸・Na
水溶性高分子の濃度（w/v%）	0.5	0.5	0.5	0.5
ε-アミノカプロン酸（w/v%）	0.5	0.5	0.5	0.5
NaOH、HCl	適量	適量	適量	適量
pH	5.5	5.5	5.5	5.5
調製時の性状	黄色澄明	調製不可	黄色澄明	調製不可
結晶析出遅延度	-50		-75	

No.	32	33	8
区分	比較例	比較例	比較例
DPY（w/v%）	0.05	0.05	0.05
サッカリン・Na（w/v%）	0.2	-	0.2
PEG4000（w/v%）	2.4	-	2.4
水溶性高分子の種類	ｶﾙﾎﾞｷｼﾋﾞﾆﾙﾎﾟﾘﾏｰ	ｶﾙﾎﾞｷｼﾋﾞﾆﾙﾎﾟﾘﾏｰ	-
水溶性高分子の濃度（w/v%）	0.1	0.1	-
ε-アミノカプロン酸（w/v%）	0.5	0.5	0.5
NaOH、HCl	適量	適量	適量
pH	5.5	5.5	5.5
調製時の性状	黄色澄明	調製不可	黄色澄明
結晶析出遅延度	-33		

[0028]DPY (1 mg or 0.5g) and PEG4000 (0.1g or 10g) were added and agitated to embodiment 6 sterile-purified-water 50mL. It added and dissolved until pH became three or less about the hydrochloric acid of 1N here. Saccharin and Na (10 mg or 20g), or AcTrp (10 mg or 20g) was added, and NaOH of 5N was added until all addition ingredients dissolved. Then, 0.5 g of epsilon-aminocaproic acid was added, and the hydrochloric acid of 3N was added after the churning dissolution until pH was set to 5.5. 4 W/V% of SM-15 was set to 100mL here by 12.5mL or doing 2.5mL addition of and adding sterile purified water after mixture.The prepared liquid was filtered with the membrane filter with the aperture of 0.45 micrometer, the vial was filled up, and it was considered as the aqueous formulation (formula No.34, 35, 38, 39) of this invention. 10 mg DPY and PEG4000 [2.4-g] were added and agitated to sterile-purified-water 50mL. It added and dissolved until pH became three or less about the hydrochloric acid of 1N here. 12.5mL addition of 12.4mL and 4 W/V% of SM-15 was carried out, and the churning dissolution of saccharin and Na 3.1-g, or the 25 W/V%AcTrp solution was carried out. 100mL was used by adding NaOH of 1N until pH is set to 10.0, and adding sterile purified water. The prepared liquid was filtered with the membrane filter with the aperture of 0.45 micrometer, the vial was filled up, and it was considered as the aqueous formulation (formula No.37, 41) of this invention. 4.0-g SM-15 was added to hot water 70mL, and it agitated under ice-cooling after distribution until SM-15 dissolved. After adding and agitating 0.05 g DPY and PEG4000 [2.4-g] here, it added and the hydrochloric acid of 1N was dissolved until pH became three or less. 12.4mL and 0.5 g of epsilon-aminocaproic acid were added, and the churning dissolution of saccharin and Na 3.1-g, or the 25 W/V%AcTrp solution was carried out. NaOH of 1N or the hydrochloric acid of 1N adjusted pH to 5.5, and it was made 100mL by adding sterile purified water. The prepared liquid was filtered with the membrane filter with the aperture of 0.45 micrometer, the vial was filled up, and it was considered as the aqueous formulation (formula No.36, 40) of this invention. NFLX (10-mg or 3g) and PEG4000 (0.1g, 2.4g, or 10g) was added and agitated to sterile-purified-water 50mL. It added and dissolved until pH became four or less about the hydrochloric acid of 1N here. AcTrp (10 mg, 3.1g, or 20g) was added, and NaOH of 5N was added until all addition ingredients dissolved. Then, 4 W/V% of SM-15 was set to 100mL by 5mL or doing 12.5mL addition of, and NaOH of 1N or the hydrochloric acid of 1N adjusting pH to 7.0 or 8.5 after mixture uniformly, and adding sterile purified water. The prepared liquid was filtered with the membrane filter with the aperture of 0.45 micrometer, the vial was filled up, and it was considered as the aqueous formulation (formula No.42, 43, 45) of this invention. 4.0-g SM-15 was added to hot water 70mL, and it agitated under ice-cooling after distribution until SM-15 dissolved. It added and dissolved here until it added 0.3 g NFLX and PEG4000 [2.4-g] and pH became five or less about the hydrochloric acid of 1N after churning. 12.4mL was added for 25 W/V%AcTrp solution, NaOH of 1N or the hydrochloric acid of 1N adjusted pH to 6.5 after mixture uniformly, and it was made 100mL by adding sterile purified water. The prepared liquid was filtered with the membrane filter with the aperture of 0.45 micrometer, the vial was filled up, and it was considered as the aqueous formulation (formula No.44) of this invention. The prepared aqueous formulation of this invention was saved for three months at 25 **. As for precipitation of a slightly soluble medicine, each tablet was not seen after preservation,

but it was stable. The result was shown in table-6.
[0029]
[Table-6]
表－6

No.	34	35	36	37
DPY (w/v%)	0.5	0.001	0.05	0.01
サッカリン・Na (w/v%)	20	0.01	3.1	3.1
PEG4000 (w/v%)	10	0.1	2.4	2.4
SM-15 (w/v%)	0.5	0.1	4.0	0.5
ε-アミノカプロン酸 (w/v%)	0.5	0.5	0.5	-
NaOH、HCl	適量	適量	適量	適量
pH	5.5	5.5	5.5	10.0
調製時の性状	黄色澄明	黄色澄明	黄色澄明	黄色澄明
25℃保存3ヶ月後の性状	変化なし	変化なし	変化なし	変化なし

No.	38	39	40	41
DPY (w/v%)	0.5	0.001	0.05	0.01
AcTrp (w/v%)	20	0.01	3.1	3.1
PEG4000 (w/v%)	10	0.1	2.4	2.4
SM-15 (w/v%)	0.5	0.1	4.0	0.5
ε-アミノカプロン酸 (w/v%)	0.5	0.5	0.5	-
NaOH、HCl	適量	適量	適量	適量
pH	5.5	5.5	5.5	10.0
調製時の性状	黄色澄明	黄色澄明	黄色澄明	黄色澄明
25℃保存3ヶ月後の性状	変化なし	変化なし	変化なし	変化なし

No.	42	43	44	45
NFLX (w/v%)	3.0	0.01	0.3	0.01
AcTrp (w/v%)	20	0.01	3.1	3.1
PEG4000 (w/v%)	10	0.1	2.4	2.4
SM-15 (w/v%)	0.2	0.2	4.0	0.5
NaOH、HCl	適量	適量	適量	適量
pH	7.0	7.0	6.5	8.5
調製時の性状	黄色澄明	無色澄明	無色澄明	無色澄明
25℃保存3ヶ月後の性状	変化なし	変化なし	変化なし	変化なし

[0030]DPY (0.2-0.5g), saccharin and Na (10-50g), PEG4000 (20g), the chlorobutanol (4g), and NaCl (2.3g) were added and agitated to embodiment 7 sterile-purified-water 500mL. It added and dissolved until pH became three or less about the hydrochloric acid of 1N here. 125mL and 4 g of epsilon-aminocaproic acid were added, and the churning dissolution of 4 W/V%SM-15 was carried out. NaOH of 1N or the hydrochloric acid of 1N adjusted pH to 5.5, and it was made 1000mL by adding sterile purified water. The prepared liquid was filtered with the membrane filter with the aperture of 0.2 micrometer, the instillation bottle made from plastics of 5mL was filled up, and it was considered as the DPY content aqueous eye drop (formula No.46-50) of this invention. The prepared ophthalmic solution of this invention was saved for three months at 25 ** or 7 **. As for precipitation of a slightly soluble medicine, each tablet was not seen after preservation, but it was stable. The result was shown in table-7.
[0031]
[Table-7]

表－7

No.	46	47	48	49	50
DPY（w/v%）	0.02	0.03	0.04	0.05	0.05
サッカリン・Na（w/v%）	1.0	2.0	2.0	2.0	5.0
PEG4000（w/v%）	2.0	2.0	2.0	2.0	2.0
SM-15（w/v%）	0.5	0.5	0.5	0.5	0.5
ε-アミノカプロン酸（w/v%）	0.4	0.4	0.4	0.4	0.4
クロロブタノール（w/v%）	0.4	0.4	0.4	0.4	0.4
NaCl	0.23	0.23	0.23	0.23	0.23
NaOH、HCl	適量	適量	適量	適量	適量
pH	5.5	5.5	5.5	5.5	5.5
調製時の性状	黄色澄明	黄色澄明	黄色澄明	黄色澄明	黄色澄明
25℃保存3ヶ月後の性状	変化なし	変化なし	変化なし	変化なし	変化なし
7℃保存3ヶ月後の性状	変化なし	変化なし	変化なし	変化なし	変化なし

[0032]3-g NFLX, ofloxacin (it is hereafter called OFLX for short) or lomefloxacin (it is hereafter called LFLX for short), and PEG4000 [24-g] were added and agitated to embodiment 8 sterile-purified-water 500mL. It added and dissolved until pH became five or less about the hydrochloric acid of 1N here. NaOH of 1N or 1N hydrochloric acid adjusted pH to 7.0 after mixture until it carried out 160mL addition of the 25 W/V%AcTrp solution and became uniform at the pan, and it was made 1000mL by adding sterile purified water. The prepared liquid was filtered with the membrane filter with the aperture of 0.2 micrometer, the instillation bottle made from plastics of 5mL was filled up, and it was considered as the DPY content aqueous eye drop (formula No.51, 52, 53) of this invention. The prepared ophthalmic solution of this invention was saved for three months at 25 ** or 7 **. As for precipitation of a slightly soluble medicine, each tablet was not seen after preservation, but it was stable. The result was shown in table-8.
[0033]
[Table-8]
表－8

No.	51	52	53
薬物	OFLX	LFLX	NFLX
薬物濃度（w/v%）	0.3	0.3	0.3
AcTrp（w/v%）	2.5	2.5	2.5
PEG4000（w/v%）	2.4	2.4	2.4
SM-15（w/v%）	0.5	0.5	0.5
NaOH、HCl	適量	適量	適量
pH	7.0	7.0	7.0
調製時の性状	無色澄明	無色澄明	無色澄明
25℃保存3ヶ月後の性状	変化なし	変化なし	変化なし
7℃保存3ヶ月後の性状	変化なし	変化なし	変化なし

[0034]
[Effect of the Invention]The slightly soluble medicine is dissolving in water in neutral vicinity, and the slightly soluble medicine content aqueous formulation of this invention does not have generating of a crystal or a foreign substance, either, and is excellent in preservation stability.